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|---|---|---|
| NEWS 1 | | Web Page URLs for STN Seminar Schedule - N. America |
| NEWS 2 | Apr 08 | "Ask CAS" for self-help around the clock |
| NEWS 3 | Apr 09 | BEILSTEIN: Reload and Implementation of a New Subject Area |
| NEWS 4 | Apr 09 | ZDB will be removed from STN |
| NEWS 5 | Apr 19 | US Patent Applications available in IFICDB, IFIPAT, and IFIUDB |
| NEWS 6 | Apr 22 | Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS |
| NEWS 7 | Apr 22 | BIOSIS Gene Names now available in TOXCENTER |
| NEWS 8 | Apr 22 | Federal Research in Progress (FEDRIP) now available |
| NEWS 9 | Jun 03 | New e-mail delivery for search results now available |
| NEWS 10 | Jun 10 | MEDLINE Reload |
| NEWS 11 | Jun 10 | PCTFULL has been reloaded |
| NEWS 12 | Jul 02 | FOREGE no longer contains STANDARDS file segment |
| NEWS 13 | Jul 22 | USAN to be reloaded July 28, 2002;<br>saved answer sets no longer valid |
| NEWS 14 | Jul 29 | Enhanced polymer searching in REGISTRY |
| NEWS 15 | Jul 30 | NETFIRST to be removed from STN |
| NEWS 16 | Aug 08 | CANCERLIT reload |
| NEWS 17 | Aug 08 | PHARMAMarketLetter(PHARMAML) - new on STN |
| NEWS 18 | Aug 08 | NTIS has been reloaded and enhanced |
| NEWS 19 | Aug 19 | Aquatic Toxicity Information Retrieval (AQUIRE)<br>now available on STN |
| NEWS 20 | Aug 19 | IFIPAT, IFICDB, and IFIUDB have been reloaded |
| NEWS 21 | Aug 19 | The MEDLINE file segment of TOXCENTER has been reloaded |
| NEWS 22 | Aug 26 | Sequence searching in REGISTRY enhanced |
| NEWS 23 | Sep 03 | JAPIO has been reloaded and enhanced |
| NEWS 24 | Sep 16 | Experimental properties added to the REGISTRY file |
| NEWS 25 | Sep 16 | CA Section Thesaurus available in CAPLUS and CA |
| NEWS 26 | Oct 01 | CASREACT Enriched with Reactions from 1907 to 1985 |
| NEWS 27 | Oct 21 | EVENTLINE has been reloaded |
| NEWS 28 | Oct 24 | BEILSTEIN adds new search fields |
| NEWS 29 | Oct 24 | Nutraceuticals International (NUTRACEUT) now available on STN |
| NEWS 30 | Oct 25 | MEDLINE SDI run of October 8, 2002 |
| NEWS 31 | Nov 18 | DKILIT has been renamed APOLLIT |
| NEWS 32 | Nov 25 | More calculated properties added to REGISTRY |
| NEWS 33 | Dec 02 | TIBKAT will be removed from STN |
| NEWS 34 | Dec 04 | CSA files on STN |
| NEWS 35 | Dec 17 | PCTFULL now covers WP/PCT Applications from 1978 to date |
| NEWS 36 | Dec 17 | TOXCENTER enhanced with additional content |
| NEWS 37 | Dec 17 | Adis Clinical Trials Insight now available on STN |
| NEWS 38 | Dec 30 | ISMEC no longer available |

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NEWS 39   Jan 13   Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 40   Jan 21   NUTRACEUT offering one free connect hour in February 2003
NEWS 41   Jan 21   PHARMAML offering one free connect hour in February 2003
NEWS 42   Jan 29   Simultaneous left and right truncation added to COMPENDEX,
                   ENERGY, INSPEC
NEWS 43   Feb 13   CANCERLIT is no longer being updated
NEWS 44   Feb 24   METADEX enhancements
NEWS 45   Feb 24   PCTGEN now available on STN
NEWS 46   Feb 24   TEMA now available on STN
NEWS 47   Feb 26   NTIS now allows simultaneous left and right truncation
NEWS 48   Feb 26   PCTFULL now contains images
NEWS 49   Mar 04   SDI PACKAGE for monthly delivery of multifile SDI results

NEWS EXPRESS  January 6 CURRENT WINDOWS VERSION IS V6.01a,
              CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
              AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
NEWS HOURS    STN Operating Hours Plus Help Desk Availability
NEWS INTER    General Internet Information
NEWS LOGIN    Welcome Banner and News Items
NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
NEWS WWW      CAS World Wide Web Site (general information)

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=> s squalene(w)epoxidase and HMG-CoA(w)reductase
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L1 85 SQUALENE(W) EPOXIDASE AND HMG-COA(W) REDUCTASE

=> duplicate remove l1
DUPLICATE PREFERENCE IS 'AGRICOLA, BIOSIS, EMBASE, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L1
L2 55 DUPLICATE REMOVE L1 (30 DUPLICATES REMOVED)

=> d l2 1-10 ti

L2 ANSWER 1 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
TI Squalene synthase inhibitors suppress triglyceride biosynthesis through the farnesol pathway in rat hepatocytes.

L2 ANSWER 2 OF 55 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 2
TI ***Squalene*** ***epoxidase*** as hypocholesterolemic drug target revisited.

L2 ANSWER 3 OF 55 CAPLUS COPYRIGHT 2003 ACS
TI Methods of treating syndrome x with aliphatic polyamines

L2 ANSWER 4 OF 55 CAPLUS COPYRIGHT 2003 ACS
TI Preparation of bicyclic diamines as CCR2 and CCR3 chemokine receptor antagonists for treating/preventing diseased associated with monocyte, lymphocyte or leukocyte accumulation

L2 ANSWER 5 OF 55 CAPLUS COPYRIGHT 2003 ACS
TI Devices and compositions containing enzyme inhibitors for cholesterol management

L2 ANSWER 6 OF 55 CAPLUS COPYRIGHT 2003 ACS
TI PPAR agonists, e.g., 3-[4-[2-[3-(2,4-dimethoxyphenyl)-1-heptylureido]ethyl]phenyl]-2-ethoxypropionic acid and analogs, useful particularly as PPAR.alpha. agonists, and their pharmaceutical compositions and therapeutic use as hypolipemics, antidiabetics, etc.

L2 ANSWER 7 OF 55 CAPLUS COPYRIGHT 2003 ACS
TI Transgenic plants carrying expression constructs for seed-specific biosynthesis of sterols and tocopherols

L2 ANSWER 8 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
TI Inhibition of cholesterol synthesis causes both hypercholesterolemia and hypocholesterolemia in hamsters.

L2 ANSWER 9 OF 55 CAPLUS COPYRIGHT 2003 ACS
TI Ovulatory surges of human CG prevent hormone-induced granulosa cell tumor formation leading to the identification of tumor-associated changes in the transcriptome

L2 ANSWER 10 OF 55 CAPLUS COPYRIGHT 2003 ACS
TI Diet-induced obesity and hepatic gene expression alterations in C57BL/6J and ICAM-1-deficient mice

=> s l2 and plant

L3 2 L2 AND PLANT

=> s l2 and (soybean or maize or arabidopsis)
L4 1 L2 AND (SOYBEAN OR MAIZE OR ARABIDOPSIS)

=> d l3 1-2 ibib ab

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:594997 CAPLUS
DOCUMENT NUMBER: 137:152492
TITLE: Transgenic ***plants*** carrying expression constructs for seed-specific biosynthesis of sterols and tocopherols
INVENTOR(S): Karunanandaa, Balasulojini; Post-Beittenmiller, Martha; Venkatramesh, Mylavarapu; Kishore, Ganesh M.; Thorne, Gregory M.; Ledeaux, John
PATENT ASSIGNEE(S): Monsanto Technology L.L.C., USA
SOURCE: PCT Int. Appl., 271 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002061072 | A2 | 20020808 | WO 2002-US255 | 20020104 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| PRIORITY APPLN. INFO.: | | | |
|---|---|---|---|
| US 2001-260114P | P | 20010105 | |
| US 2001-885723 | A | 20010620 | |

AB Expression constructs for 3-hydroxy-3-methylglutaryl-CoA reductase and at least one other enzyme of sterol biosynthesis are described for use in the engineering of patterns of sterol biosynthesis. Also disclosed are methods for using such constructs to alter sterol prodn. and content in cells, ***plants*** , seeds and storage organs of ***plants*** . Also provided are oils and compns. contg. altered sterol levels produced by use of the disclosed constructs. Novel nucleotide sequences useful in the alteration of sterol prodn. are also provided. Also provided are cells, ***plants*** , seeds and storage organs of ***plants*** comprising sequences encoding 3-hydroxy-3-methylglutaryl-CoA reductase, at least one other sterol synthesis pathway enzyme and at least one tocopherol synthesis enzyme.

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:453094 CAPLUS
DOCUMENT NUMBER: 135:72153
TITLE: Moss genes from Physcomitrella patens encoding proteins involved in the synthesis of tocopherols and

carotenoids

INVENTOR(S): Lerchl, Jens; Renz, Andreas; Ehrhardt, Thomas; Reindl, Andreas; Cirpus, Petra; Bischoff, Friedrich; Frank, Markus; Freund, Annette; Duwenig, Elke; Schmidt, Ralf-Michael; Reski, Ralf; Badur, Ralf
PATENT ASSIGNEE(S): Basf Plant Science G.m.b.H., Germany
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001044276 | A2 | 20010621 | WO 2000-EP12698 | 20001214 |
| WO 2001044276 | A3 | 20011108 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| BR 2000016432 | A | 20020917 | BR 2000-16432 | 20001214 |
| EP 1244696 | A2 | 20021002 | EP 2000-983319 | 20001214 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |

PRIORITY APPLN. INFO.: US 1999-171121P P 19991216
WO 2000-EP12698 W 20001214

AB Isolated nucleic acid mols., designated TCMRP (Tocopherol and Carotenoid Metab. Related Protein) nucleic acid mols., which encode novel TCMRPs from e.g. Physcomitrella patens are described. The invention also provides antisense nucleic acid mols., recombinant expression vectors contg. TCMRP nucleic acid mols., and host cells into which the expression vectors have been introduced. The invention still further provides isolated TCMRPs, mutated TCMRPs, fusion proteins, antigenic peptides and methods for the improvement of prodn. of a desired compd. from transformed cells, organisms or ***plants*** based on genetic engineering of TCMRP genes in these organisms.

=> s s transform? and squalene(w)epoxidase and HMG-COA(w)reductase
L5 0 S TRANSFORM? AND SQUALENE(W) EPOXIDASE AND HMG-COA(W) REDUCTASE

=> s transform? and squalene(w)epoxidase and HMG-COA(w)reductase
L6 3 TRANSFORM? AND SQUALENE(W) EPOXIDASE AND HMG-COA(W) REDUCTASE

=> d l6 1-3 ti

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS
TI Moss genes from Physcomitrella patens encoding proteins involved in the synthesis of tocopherols and carotenoids

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS

TI Method for producing ergosterol and intermediates by recombinant yeast fermentation

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS
TI Cholesterol-lowering 2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylic acid derivatives with squalene synthetase inhibitory activity, also useful as antifungal and anticancer agents

=> d l6 2 ibbi ab
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PATS -------- PI, SO
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SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers; SCAN must be entered on the same line as the DISPLAY, e.g., D SCAN or DISPLAY SCAN)
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IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

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OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

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HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT) containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its

structure diagram, plus NTE and SEQ fields
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OCC --------- Number of occurrence of hit term and field in which it occurs

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L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS

| | |
|---|---|
| ACCESSION NUMBER: | 1999:234007 CAPLUS |
| DOCUMENT NUMBER: | 130:280919 |
| TITLE: | Method for producing ergosterol and intermediates by recombinant yeast fermentation |
| INVENTOR(S): | Weber, Alfred; Klages, Uwe; Kennecke, Mario; Lang, Christine; Stahl, Ulf; Polakowski, Thomas |
| PATENT ASSIGNEE(S): | Schering A.-G., Germany |
| SOURCE: | PCT Int. Appl., 45 pp.<br>CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | German |
| FAMILY ACC. NUM. COUNT: | 1 |
| PATENT INFORMATION: | |

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9916886 | A1 | 19990408 | WO 1998-EP6134 | 19980928 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 19744212 | A1 | 19990415 | DE 1997-19744212 | 19970930 |
| CA 2305780 | AA | 19990408 | CA 1998-2305780 | 19980928 |
| AU 9911474 | A1 | 19990423 | AU 1999-11474 | 19980928 |
| AU 750768 | B2 | 20020725 | | |
| EP 1015597 | A1 | 20000705 | EP 1998-954286 | 19980928 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001518301 | T2 | 20011016 | JP 2000-513955 | 19980928 |
| NO 2000001625 | A | 20000329 | NO 2000-1625 | 20000329 |
| PRIORITY APPLN. INFO.: | | | DE 1997-19744212 A | 19970930 |
| | | | WO 1998-EP6134 W | 19980928 |

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 16 2 ab

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS
AB The invention concerns the prodn. of ergosterol in yeast by constructing plasmids with the ergosterol biosynthesis genes; ***transformation*** , expression of the genes in yeast cells, fermn.; and isolation of ergosterol and its intermediates in chromatog. columns. Plasmids are constructed contg. single genes or their combination. The following genes are involved: t-HMG, coding for HMG-Co-A-Reductase; ERG9, coding for squalene synthetase; SAT1, coding for Acyl-CoA:Sterol-acetyltransferase; and ERG1, coding for ***squalene*** ***epoxidase*** . A DNA sequence coding for tHMG was amplified from genomic DNA of Saccharomyces cerevisiae using tHMG-5' and tHMG-3' primers. The DNA fragment was inserted into the pUC19 cloning vector; the pUC19-tHMG plasmid was isolated, ligated with yeast expression vector pPT2b. The obtained pPT2b-tHMG vector contained the ADH1 promoter, the tHMG fragment and the TRP1 terminator; it was cleaved at the EcoRV and Nrul site; the fragment contg. the middle part of ADH1, tHMG and TRP1 terminator was inserted into in the YEp13 yeast vector. The resulting YEpH2 vector included the tetracycline resistance gene, the middle part of the ADH1 promoter, the tHMG and the TRP1 terminator; it was inserted into the YDpU vector resulting YDpUH2/12; ligated to the kanamycin resistance gene; the result was the YDpUHK3 construct. The S. cerevisiae AH22 strain was ***transformed*** with the construct; resulting in an integration at the URA3 gene locus. ***Transformed*** yeast cells underwent FOA selection; the uracil auxotrophic strain AH22/tH3ura8 was isolated that contained the tHMG1 expression cassette in chromosomal integration at the URA3 gene. Fermn. of the ***transformed*** yeast resulted increased ***HMG*** - ***CoA*** - ***reductase*** activity; increased squalene and ergosterol prodn. compared to the non- ***transformed*** AH22 cells. Similar procedure resulted the ***transformed*** AH22/pADL-SAT1 yeast cells that contained the SAT1 gene in the pADL-SAt1 expression vector. Fermn. of the AH22/pADL-SAT1 resulted in no squalene and increased ergosterol compared to the non- ***transformed*** strain. The pADL-SAt1 expression vector was inserted into ***transformed*** AH22/tH3ura8 cells; the resulting AH22/tH3ura8/pADL-SAT1 yeast cells produced 5.540 wt./wt.% ergosterol compared with 3.798 wt./wt.% produced by the AH22/tH3ura8 (expressed in % of yeast dry mass). The optimum uracil concn. in the culture medium was 20 .mu.g/mL. Varying the culture media compn., the concn. of the intermediates changes; thus different concns. of lanosterol, 4,4-dimethylzymosterol, zymosterol, ergost-7-enol, and ergosta-5,7-dienol were obtained. The AH22/tH3ura8/pADL-SAT1 strains produced mainly lanosterol and 4,4-dimethylzymosterol as intermediates.

=> d l6 1 ibib ab

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:453094 CAPLUS
DOCUMENT NUMBER: 135:72153
TITLE: Moss genes from Physcomitrella patens encoding proteins involved in the synthesis of tocopherols and carotenoids
INVENTOR(S): Lerchl, Jens; Renz, Andreas; Ehrhardt, Thomas; Reindl, Andreas; Cirpus, Petra; Bischoff, Friedrich; Frank,

Markus; Freund, Annette; Duwenig, Elke; Schmidt, Ralf-Michael; Reski, Ralf; Badur, Ralf
PATENT ASSIGNEE(S): Basf Plant Science G.m.b.H., Germany
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001044276 | A2 | 20010621 | WO 2000-EP12698 | 20001214 |
| WO 2001044276 | A3 | 20011108 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|
| BR 2000016432 | A | 20020917 | BR 2000-16432 | 20001214 |
| EP 1244696 | A2 | 20021002 | EP 2000-983319 | 20001214 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:
US 1999-171121P P 19991216
WO 2000-EP12698 W 20001214

AB Isolated nucleic acid mols., designated TCMRP (Tocopherol and Carotenoid Metab. Related Protein) nucleic acid mols., which encode novel TCMRPs from e.g. Physcomitrella patens are described. The invention also provides antisense nucleic acid mols., recombinant expression vectors contg. TCMRP nucleic acid mols., and host cells into which the expression vectors have been introduced. The invention still further provides isolated TCMRPs, mutated TCMRPs, fusion proteins, antigenic peptides and methods for the improvement of prodn. of a desired compd. from ***transformed*** cells, organisms or plants based on genetic engineering of TCMRP genes in these organisms.

=> d l6 3 ibib ab

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:234418 CAPLUS
DOCUMENT NUMBER: 118:234418
TITLE: Cholesterol-lowering 2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylic acid derivatives with squalene synthetase inhibitory activity, also useful as antifungal and anticancer agents
INVENTOR(S): Parsons, William H.; Biftu, Tesfaye; Acton, John J., III; Bugianesi, Robert L.; Berger, Gregory D.; Burk, Robert M.; Girotra, Narindar N.; Ponpipom, Mitree M.; Kuo, Chan Hwa; et al.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 270 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 512865 | A2 | 19921111 | EP 1992-304187 | 19920508 |
| EP 512865 | A3 | 19921202 | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE

PRIORITY APPLN. INFO.: US 1991-698766 19910510
US 1991-805602 19911209
US 1992-866749 19920415

OTHER SOURCE(S): MARPAT 118:234418

AB Title compds. I [a = 0, 1; A = CO, NR3CO, OC(O); R1 = (substituted and/or heteroatom-replaced) alkyl or alkenyl, (substituted) (hetero)aryl, (substituted) cycloalkyl; R2 = alkyl, alkenyl, alkynyl, (substituted) (hetero)aryl or (hetero)aralkyl, heterocycloalkylalkyl, (substituted) aralkenyl; R3 = H, alkenyl, alkynyl, (substituted) alkyl, (hetero)aryl, (hetero)aralkyl, or heterocycloalkylalkyl; R4 = H, (substituted and/or heteroatom-replaced) alkyl or alkenyl, (substituted) (hetero)aryl or cycloalkyl; R5 = H, (cyclo)alkyl, (substituted) aryl or aralkyl, R2OC(O), R3C(O), R3R3NC(O); R6, R6a = H, (substituted and/or heteroatom-replaced) alkyl, alkenyl, or alkynyl, (substituted) (hetero)aryl or cycloalkyl; Z1, Z2, Z3 = OR6a, SR6a, NR6aR6a; some provisos], which are semisynthetic analogs of natural products, were prepd. as squalene synthetase-inhibiting antihypercholesterolemics with addnl. activities. For example, natural product II [R4(A)a = (4S,6S)-dimethyl-2-octenoyl], isolated by culturing MF5453 (ATCC 20986), was subjected to a sequence of (1) conversion to the tris-tert-Bu ester, (2) addnl. protection as the 7-O-(1-methyl-1-methoxyethyl) ether, (3) selective basic hydrolysis to give the 6-OH compd., (4) reaction of the 6-OH with an appropriate isocyanate, and (5) deprotection with CF3CO2H, to give II [R4 = PhO(CH2)11, A = NHCO, a = 1] (III). The IC50 of III for inhibition of squalene synthetase in vitro was 0.24 .mu.M. I also inhibited farnesylation of the oncogene protein Ras, and showed broad-spectrum antifungal activity in vitro.

=> s steroid(w)pathway and biosynthesis and transg?
L7 0 STEROID(W) PATHWAY AND BIOSYNTHESIS AND TRANSG?

=> s steroid(w)pathway and biosynthesis and trans?
3 FILES SEARCHED...
L8 0 STEROID(W) PATHWAY AND BIOSYNTHESIS AND TRANS?

=> s steroid(w)pathway and biosynthesis and plant
L9 3 STEROID(W) PATHWAY AND BIOSYNTHESIS AND PLANT

=> d l9 1-3 ti

L9 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI Selection and characterisation of variant Solanum xanthocarpum that overproduce steroids.

L9 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI Enzymes in cardenolide-accumulating shoot cultures of Digitalis purpurea L.

L9 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS
TI Selection and characterization of variant Solanum xanthocarpum that overproduce steroids

=> d l9 1-2 ibib ab

L9 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:453976 BIOSIS
DOCUMENT NUMBER: PREV199800453976
TITLE: Selection and characterisation of variant Solanum xanthocarpum that overproduce steroids.
AUTHOR(S): Josekutty, P. C. (1)
CORPORATE SOURCE: (1) Dep. Botany, Univ. Transkei, Private Bag X1, Umtata, Eastern Cape South Africa
SOURCE: Phyton (Buenos Aires), (1998) Vol. 62, No. 1-2, pp. 125-130.
ISSN: 0031-9457.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Variant cell lines of Solanum xanthocarpum Shrader and Wendl. resistant to mevinolin, a specific inhibitor of HMGR (3-hydroxy 3-methylglutaryl Coenzyme A Reductase) was selected using the cell plating technique. The selected cell line exhibited more than 2.0 fold the sterols and 3.0 fold the steroidal alkaloid solasodine compared to the control. ***Plants*** regenerated from the mutant cell line recorded 150% more sterols and 200% more steroidal alkaloid solasodine than the wild type regenerants. Leaf disc assay of the regenerated ***plants*** showed resistance to otherwise lethal concentrations of mevinolin. These results point to an important regulatory role of HMGR in the ***steroid*** ***pathway*** . Present study shows development of a variant higher ***plant*** and cell line which overproduce steroids and is thus useful for further studies on the regulation of phytosterol ***biosynthesis*** .

L9 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:132212 BIOSIS
DOCUMENT NUMBER: PREV199598146512
TITLE: Enzymes in cardenolide-accumulating shoot cultures of Digitalis purpurea L.
AUTHOR(S): Seitz, Hanns Ulrich; Gaertner, Dorothea Elisabeth
CORPORATE SOURCE: Bot. Inst., Univ. Tuebingen, Auf Morgenstelle 1, D-72076 Tuebingen Germany
SOURCE: Plant Cell Tissue and Organ Culture, (1994) Vol. 38, No. 2-3, pp. 337-344.
ISSN: 0167-6857.
DOCUMENT TYPE: Article
LANGUAGE: English
AB In contrast to undifferentiated cell suspension cultures of Digitalis lanata, photomixotrophic shoot cultures of Digitalis purpurea accumulate cardiac glycosides in substantial concentrations. They are used to investigate enzymes of the cardenolide pathway. All cardenolides are 53-configurated. The progesterone 5-beta-reductase and the 3-beta-hydroxysteroid-5-beta-oxidoreductase are present in shoot cultures but not in undifferentiated cell cultures. These enzymes provide precursors for cardenolides, whereas the presence of the progesterone 5-alpha-reductase, also present in shoot cultures, is discussed with

regard to its role in phytosterol ***biosynthesis*** and may be attributed to the general ***steroid*** ***pathway*** . The progesterone 5-alpha-reductase had an activity maximum during the early growth period seven days after onset of cultivation, whereas the corresponding progesterone 5-beta-reductase activity was highest on day II. The maximum cardenolide accumulation was after 24 days. The enzyme activities present in crude extracts from shoot cultures were characterized with regard to their requirements for NADPH and NADH, pH-optimum, temperature optimum, affinity to their substrates and their localization in the cell. The progesterone 5-beta-reductase was purified 769-fold.

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=> s HMG-CoA(w)reductase and rate(w)limiting
L10          747 HMG-COA(W) REDUCTASE AND RATE(W) LIMITING

=> s HMG-CoA(w)reductase and rate(w)limiting and plant
L11           22 HMG-COA(W) REDUCTASE AND RATE(W) LIMITING AND PLANT

=> duplicate remove l11
DUPLICATE PREFERENCE IS 'BIOSIS, EMBASE, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L11
L12           16 DUPLICATE REMOVE L11 (6 DUPLICATES REMOVED)

=> d l12 1-16 ti

L12  ANSWER 1 OF 16  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE
     1
TI     ***Plant***  -derived monoterpenes suppress hamster kidney cell
     3-hydroxy-3-methylglutaryl coenzyme a reductase synthesis at the
     post-transcriptional level.

L12  ANSWER 2 OF 16  CAPLUS  COPYRIGHT 2003 ACS
TI   Cloning and bacterial expression of a 3-hydroxy-3-methylglutaryl-CoA
     reductase cDNA (HMG1) from peel tissue of apple fruit

L12  ANSWER 3 OF 16  CAPLUS  COPYRIGHT 2003 ACS
TI   Increasing isoprenoid biosynthesis in  ***plants***  by recombinant
     expression of modified  ***HMG*** - ***CoA***  ***reductase***
     with no regulation by protein kinase phosphorylation

L12  ANSWER 4 OF 16  EMBASE  COPYRIGHT 2003 ELSEVIER SCI. B.V.
TI   The mechanism underlying the hypocholesterolaemic activity of aqueous
     celery extract, its butanol and aqueous fractions in genetically
     hypercholesterolamic RICO rats.

L12  ANSWER 5 OF 16  CAPLUS  COPYRIGHT 2003 ACS
TI   Regulation by HMGR of sterol biosynthesis in a selected high sterol cell
     line of Solanum xanthocarpum Shrader & Wendl

L12  ANSWER 6 OF 16  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI   Overexpression of a cytosolic hydroxymethylglutaryl-CoA reductase leads to
     squalene accumulation in yeast.

L12  ANSWER 7 OF 16  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI   Effects of overproduction of the catalytic domain of 3-hydroxy-3-
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methylglutaryl coenzyme A reductase on squalene synthesis in Saccharomyces cerevisiae.

L12 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2003 ACS
TI Screening and characterization of anticholesterogenic substances from food ***plant*** extracts

L12 ANSWER 9 OF 16 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI Different subcellular localization of Saccharomyces cerevisiae ***HMG*** - ***CoA*** ***reductase*** isozymes at elevated levels corresponds to distinct endoplasmic reticulum membrane proliferations.

L12 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
TI A high activity of 3-hydroxy-3-methylglutaryl coenzyme A reductase in chloroplasts of Stevia rebaudiana Bertoni.

L12 ANSWER 11 OF 16 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI Positive and negative regulation of a sterol biosynthetic gene (ERG3) in the post-squalene portion of the yeast ergosterol pathway.

L12 ANSWER 12 OF 16 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
TI ***HMG*** - ***CoA*** ***reductase*** and terpenoid phytoalexins: Molecular specialization within a complex pathway.

L12 ANSWER 13 OF 16 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
TI Effect of beta-carotene on the expression of 3-hydroxy-3-methylglutaryl coenzyme A reductase in rat liver.

L12 ANSWER 14 OF 16 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI Comparison of the effects of condensed tannin and pectin on cecal fermentations and lipid metabolism in the rat.

L12 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2003 ACS
TI Microbial production of abscisic acid, a ***plant*** hormone, by Botrytis cinerea. Studies on blue light-promoting effect on the production and the ***rate*** - ***limiting*** step in the biosynthesis

L12 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2003 ACS
TI ***Plant*** growth regulation by mevinolin and other sterol biosynthesis inhibitors

=> d l12 12 ibib ab

L12 ANSWER 12 OF 16 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
ACCESSION NUMBER: 1995:179049 BIOSIS
DOCUMENT NUMBER: PREV199598193349
TITLE: ***HMG*** - ***CoA*** ***reductase*** and terpenoid phytoalexins: Molecular specialization within a complex pathway.
AUTHOR(S): Weissenborn, Deborah L. (1); Denbow, Cynthia J.; Laine, Marko; Lang, Saara S.; Yang, Zhenbiao; Yu, Xueshu; Cramer, Carole L. (1)

CORPORATE SOURCE: (1) Dep. Plant Pathol. Physiol. Weed Sci., Va. Polytech. Inst. State Univ., Blacksburg, VA 24061-0330 USA
SOURCE: Physiologia Plantarum, (1995) Vol. 93, No. 2, pp. 393-400. ISSN: 0031-9317.
DOCUMENT TYPE: General Review
LANGUAGE: English

AB Terpenoid phytoalexins and other defense compounds play an important role in disease resistance in a variety of ***plant*** families but have been most widely studied in solanaceous species. The ***rate*** - ***limiting*** step in terpenoid phytoalexin production is mediated by 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGR), which catalyzes mevalonic acid synthesis. HMGRs are involved in the biosynthesis of a broad array of terpenoid compounds, and distinct isoforms of HMGR may be critical in directing the flux of pathway intermediates into specific end products. ***Plant*** HMGRs are encoded by a small gene family, and genomic or cDNA sequences encoding HMGR have been isolated from several ***plant*** species. In tomato, four genes encode HMGR; these genes are differentially activated during development and stress responses. One gene, hmg2, is activated in response to wounding and a variety of pathogenic agents suggesting a role in sesquiterpene phytoalexin biosynthesis. In contrast, expression patterns of tomato hmg1 suggest a role in sterol biosynthesis and cell growth. Other ***plant*** species show an analogous separation of specific HMGR isoforms involved in growth and/or housekeeping function and inducible isoforms associated with biosynthesis of phytoalexins or other specialized "natural products." We are applying a variety of cell and molecular techniques to address whether subcellular localization and/or differential expression of these isoforms are key factors in determining end product accumulation during development and defense.

=> d l12 3 ibib ab

L12 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:320136 CAPLUS
DOCUMENT NUMBER: 134:338378
TITLE: Increasing isoprenoid biosynthesis in ***plants*** by recombinant expression of modified ***HMG*** - ***CoA*** ***reductase*** with no regulation by protein kinase phosphorylation
INVENTOR(S): Halford, Nigel G.; Hey, Sandra Janet; Beale, Michael Henry
PATENT ASSIGNEE(S): University of Bristol, UK
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001031043 | A1 | 20010503 | WO 2000-GB4141 | 20001027 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: GB 1999-25453 A 19991027
AB The present invention involves introducing novel HMGR genes, in the form of mutant ***plant*** and ***plant*** /non- ***plant*** or different ***plant*** chimeric genes, into ***plants*** with the aim of increasing isoprenoid biosynthesis and/or accumulation by uncoupling HMGR from regulation by SnRKI. The NADPH-dependent redn. of 3-hydroxy-3-methylglutarylCoA (HMG-CoA) to mevalonic acid is the overall ***rate*** - ***limiting*** step for the whole sterol biosynthetic pathway. ***HMG*** - ***CoA*** ***reductase*** (3-hydroxy-3-methylglutaryl-CoA reductase or HMGR) is the enzyme which catalyzes this step and its activity is regulated through phosphorylation by a protein kinase, adenosine 5' phosphate (AMP)activated protein kinase, AMPK. AMPK is a homolog of the yeast protein kinase SNF1 and of ***plant*** SnRK1s. Transcriptional regulation of the HMGR genes can be avoided by using heterologous promoters. The inventors have shown an increase in seed sterol content, which has not been shown previously. Preferably, the modified gene product is no longer subject to regulatory phosphorylation. The or each phosphorylation site may be rendered inactive in the modified HMGR gene product by the replacement of at least one serine, threonine or tyrosine residue of the unmodified gene product with. for example, an alanine residue. The HMGR gene may be further modified to reduce transcriptional regulation. For example, the gene may be modified through the introduction of at least one heterologous promoter. The invention further provides a method for increasing pathogen, fungus and insect and mite pest resistance in ***plants*** by increasing the expression of an isoprenoid in the ***plant*** by modifying the ***plant*** as defined above.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> s HMG-CoA and isoform
L13 113 HMG-COA AND ISOFORM

=> s l13 and (maize or soybean or arabidopsis or rice or tobacco or plant or petunia or tomato)
L14 14 L13 AND (MAIZE OR SOYBEAN OR ARABIDOPSIS OR RICE OR TOBACCO OR PLANT OR PETUNIA OR TOMATO)

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DUPLICATE PREFERENCE IS 'AGRICOLA, BIOSIS, EMBASE, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L14
L15 8 DUPLICATE REMOVE L14 (6 DUPLICATES REMOVED)

=> d l15 1-8 ti

L15 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS
TI Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile

L15 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS
TI Cloning of DNA encoding a catalytic subunit of SNF1-related protein kinase-1 (SnRK1-.alpha.1), and immunological analysis of multiple forms of the kinase, in spinach leaf

L15 ANSWER 3 OF 8 AGRICOLA DUPLICATE 1
TI Molecular aspects of alpha-tocotrienol antioxidant action and cell signalling.

L15 ANSWER 4 OF 8 AGRICOLA DUPLICATE 2
TI ***Hmg*** - ***coA*** reductase gene family in cotton (Gossypium hirsutum L.): unique structural features and differential expression of hmg2 potentially associated with synthesis of specific isoprenoids in developing embryos.

L15 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
TI ***HMG*** - ***CoA*** reductase gene families that differentially accumulate transcripts in potato tubers are developmentally expressed in floral tissues.

L15 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI Positive and negative regulation of a sterol biosynthetic gene (ERG3) in the post-squalene portion of the yeast ergosterol pathway.

L15 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
TI ***HMG*** - ***CoA*** reductase and terpenoid phytoalexins: Molecular specialization within a complex pathway.

L15 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS
TI Biochemical characterization of two forms of 3-hydroxy-3-methylglutaryl-CoA reductase kinase from cauliflower (Brassica oleracea)

=> d l15 8

L15 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1994:185819 CAPLUS
DN 120:185819
TI Biochemical characterization of two forms of 3-hydroxy-3-methylglutaryl-CoA reductase kinase from cauliflower (Brassica oleracea)
AU Ball, Kathryn L.; Dale, Susan; Weekes, John; Hardie, D. Grahame
CS Biochem. Dep., Univ. Dundee, Dundee, UK
SO European Journal of Biochemistry (1994), 219(3), 743-50
CODEN: EJBCAI; ISSN: 0014-2956
DT Journal
LA English

=> d l15 8 ibib ab

L15 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:185819 CAPLUS
DOCUMENT NUMBER: 120:185819
TITLE: Biochemical characterization of two forms of 3-hydroxy-3-methylglutaryl-CoA reductase kinase from cauliflower (Brassica oleracea)
AUTHOR(S): Ball, Kathryn L.; Dale, Susan; Weekes, John; Hardie, D. Grahame
CORPORATE SOURCE: Biochem. Dep., Univ. Dundee, Dundee, UK
SOURCE: European Journal of Biochemistry (1994), 219(3), 743-50
CODEN: EJBCAI; ISSN: 0014-2956
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors recently reported the existence of a protein kinase cascade in higher ***plants*** , of which the central component is a 3-hydroxy-3-methylglutaryl( ***HMG*** -)- ***CoA*** reductase kinase functionally related to mammalian AMP-activated protein kinase [MacKintosh, R. W., Davies, S. P., Clarke, P. R., Weekes, J., Gillespie, S. G., Gibb, B. J. & Hardie, D. G. (1992) Eur. J. Biochem. 209, 923-931]. The authors have now purified this protein kinase 9000-fold from cauliflower inflorescences. During the course of this work the authors noticed a second minor form (form B) which sepd. from the major form (A) on ion exchange and gel filtration. Both forms phosphorylate the catalytic fragment of mammalian ***HMG*** - ***CoA*** reductase. Both forms are markedly inactivated by incubation with the reactive ATP analog p-fluorosulfonylbenzoyl adenosine (FSO2PhCOAdo), and also by mammalian protein phosphatase 2C, indicating that form B, like form A, is activated by phosphorylation. Form A has an apparent native mol. mass of 200 kDa by gel filtration and, after labeling with [14C]FSO2PhCOAdo, of 150 kDa by electrophoresis in non-denaturing gels. The catalytic subunit was identified as a polypeptide of 58 kDa after labeling with [14C]FSO2PhCOAdo. Form B has an apparent native mol. mass of 45 kDa by gel filtration, and was identified as a polypeptide of 45 kDa after labeling with [14C]FSO2PhCOAdo and [.gamma.-32P]ATP. Using a series of variants of the synthetic peptide substrate, the substrate specificities of the two forms are similar but not identical. Form B does not appear to be a proteolytic fragment of form A, and the authors therefore propose that it represents a closely related member of the same protein kinase sub-family.

=> d l15 1-7 ibib ab

L15 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:338762 CAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001032928 | A2 | 20010510 | WO 2000-US30474 | 20001103 |
| WO 2001032928 | A3 | 20020725 | | |

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105
US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

L15 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:470791 CAPLUS
DOCUMENT NUMBER: 136:163210
TITLE: Cloning of DNA encoding a catalytic subunit of SNF1-related protein kinase-1 (SnRK1-.alpha.1), and

immunological analysis of multiple forms of the kinase, in spinach leaf

AUTHOR(S): Crawford, Russell M.; Halford, Nigel G.; Hardie, D. Grahame

CORPORATE SOURCE: Biochemistry Department, Dundee University, Dundee, DD1 5EH, UK

SOURCE: Plant Molecular Biology (2001), 45(6), 731-741
CODEN: PMBIDB; ISSN: 0167-4412

PUBLISHER: Kluwer Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Using a PCR approach, we have cloned DNA encoding a catalytic subunit ***isoform*** (SnRK1-.alpha.1) of SNF1-related protein kinase-1 from spinach leaf. The predicted amino acid sequence falls into the SnRK1a sub-family, and is closely related to SnRK1a sequences expressed in cucumber, ***Arabidopsis*** thaliana, ***tobacco*** and potato. We have generated two affinity-purified antipeptide antibodies (anti-RASS and anti-AEF) based on the predicted amino acid sequence of spinach SnRK1-.alpha.1. They were used to analyze multiple forms of SNF1-related kinase (HRK-A, -C, -D) that were previously identified by biochem. criteria in exts. of spinach leaf. Anti-AEF appears to be specific for the SnRK1-.alpha.1 ***isoform*** , whereas anti-RASS is a "pan-.alpha." antibody that ppts. all ***isoforms*** present in spinach leaf exts. The activities of HRK-A and HRK-C can be entirely accounted for by the SnRK1-.alpha.1 catalytic subunit. By contrast, only a small proportion of HRK-D activity (ca. 20%) can be accounted for by SnRK1-.alpha.1, with the remainder presumably being due to other ***isoforms*** (SnRK1-.alpha.2) that are currently poorly defined. A 35 kDa polypeptide recognized by an antibody against the putative ***Arabidopsis*** .beta.2 subunit co-ppts. with HRK-C, but not HRK-A or D.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 8 AGRICOLA DUPLICATE 1

ACCESSION NUMBER: 2001:68149 AGRICOLA

DOCUMENT NUMBER: IND23224079

TITLE: Molecular aspects of alpha-tocotrienol antioxidant action and cell signalling.

AUTHOR(S): Packer, L.; Weber, S.U.; Rimbach, G.

SOURCE: The Journal of nutrition, Feb 2001. Vol. 131, No. 2. p. 369S-373S
Publisher: Bethesda : American Society for Nutritional Sciences.
CODEN: JONUAI; ISSN: 0022-3166

NOTE: Paper presented at the symposium: Molecular Mechanisms of Protective Effects of Vitamin E in Atherosclerosis, Experimental Biology 2000, April 16, 2000, San Diego.
Includes references

PUB. COUNTRY: Maryland; United States

DOCUMENT TYPE: Article

FILE SEGMENT: U.S. Imprints not USDA, Experiment or Extension

LANGUAGE: English

AB Vitamin E, the most important lipid-soluble antioxidant, was discovered at the University of California at Berkeley in 1922 in the laboratory of Herbert M. Evans (Science 1922, 55: 650). At least eight vitamin E ***isoforms*** with biological activity have been isolated from ***plant*** sources. Since its discovery, mainly antioxidant and

recently also cell signaling aspects of tocopherols and tocotrienols have been studied. Tocopherols and tocotrienols are part of an interlinking set of antioxidant cycles, which has been termed the antioxidant network. Although the antioxidant activity of tocotrienols is higher than that of tocopherols, tocotrienols have a lower bioavailability after oral ingestion. Tocotrienols penetrate rapidly through skin and efficiently combat oxidative stress induced by UV or ozone. Tocotrienols have beneficial effects in cardiovascular diseases both by inhibiting LDL oxidation and by down-regulating 3-hydroxyl-3-methylglutaryl-coenzyme A ( ***HMG*** ***CoA*** ) reductase, a key enzyme of the mevalonate pathway. Important novel antiproliferative and neuroprotective effects of tocotrienols, which may be independent of their antioxidant activity, have also been described.

L15 ANSWER 4 OF 8 AGRICOLA DUPLICATE 2

ACCESSION NUMBER: 2000:15075 AGRICOLA
DOCUMENT NUMBER: IND22023893
TITLE: ***Hmg*** - ***coA*** reductase gene family in cotton (Gossypium hirsutum L.): unique structural features and differential expression of hmg2 potentially associated with synthesis of specific isoprenoids in developing embryos.
AUTHOR(S): Loguercio, L.L.; Scott, H.C.; Trolinder, N.L.; Wilkins, T.A.
CORPORATE SOURCE: EMBRAPA/CNPMS, Sete Lagoas-MG, Brazil.
AVAILABILITY: DNAL (450 P699)
SOURCE: Plant and cell physiology, July 1999. Vol. 40, No. 7. p. 750-761
Publisher: Kyoto, Japan : Japanese Society of Plant Physiologists.
CODEN: PCPHA5; ISSN: 0032-0781
NOTE: Includes references
PUB. COUNTRY: Japan
DOCUMENT TYPE: Article
FILE SEGMENT: Non-U.S. Imprint other than FAO
LANGUAGE: English

AB As a first step towards understanding the biosynthesis of isoprenoids that accumulate in specialized pigment glands of cotton at the molecular level, two full-length genes (hmg1 and hmg2) were characterized encoding ***hmg*** - ***coA*** reductase (HMGR; EC 1.1.1.34), the enzyme that catalyzes the formation of a key isoprenoid precursor. Cotton hmgr genes exhibited features typical of other ***plant*** genes, however, hmg2 encodes the largest of all ***plant*** HMGR enzymes described to date. HMG2 contains several novel features that may represent functional specialization of this particular HMGR ***isoform*** . Such features include a unique 42 amino acid sequence located in the region separating the N-terminal domain and C-terminal catalytic domain, as well as an N-terminal hydrophobic domain that is not found in HMG1 or other HMGR enzymes. DNA blot analysis revealed that hmg1 and hmg2 belong to small subfamilies that probably include homeologous loci in allotetraploid cotton (Gossypium hirsutum L.). Ribonuclease protection assays revealed that hmg1 and hmg2 are differentially expressed in a developmentally- and spatially-modulated manner during morphogenesis of specialized terpenoid-containing pigment glands in embryos. Induced expression of hmg2 coincided with a possible commitment to sesquiterpenoid biosynthesis in developing embryos, although other developmental processes also requiring HMGR cannot be excluded.

L15 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
ACCESSION NUMBER: 1997:180516 BIOSIS
DOCUMENT NUMBER: PREV199799472229
TITLE: ***HMG*** - ***CoA*** reductase gene families that differentially accumulate transcripts in potato tubers are developmentally expressed in floral tissues.
AUTHOR(S): Korth, Kenneth L. (1); Stermer, Bruce A.; Bhattacharyya, Madan K.; Dixon, Richard A.
CORPORATE SOURCE: (1) Samuel Roberts Noble Foundation, Plant Biol. Div., PO Box 2180 Ardmore, OK 73402 USA
SOURCE: Plant Molecular Biology, (1997) Vol. 33, No. 3, pp. 545-551.
ISSN: 0167-4412.
DOCUMENT TYPE: Article
LANGUAGE: English
AB We isolated two full-length cDNA clones encoding 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGR) from potato (Solanum tuberosum) L. tubers. The clones, designated hmg2.2 and hmg3.3, are members of previously described gene subfamilies. In addition to being induced by arachidonic acid in tubers, hmg2.2 transcript accumulates developmentally in young flowers, and in mature sepals and ovaries, whereas transcript for hmg3.3 accumulates in mature petals and anthers. Our data suggest that members of specific HMGR-encoding gene subfamilies might be involved in both defense responses and flower development. Accumulation of different HMGR transcripts could provide some control of isoprenoid biosynthesis by producing ***isoforms*** specific for classes of end-products produced in particular tissues.

L15 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:462475 BIOSIS
DOCUMENT NUMBER: PREV199699184831
TITLE: Positive and negative regulation of a sterol biosynthetic gene (ERG3) in the post-squalene portion of the yeast ergosterol pathway.
AUTHOR(S): Arthington-Skaggs, B. A.; Crowell, D. N.; Yang, H.; Sturley, S. L.; Bard, M. (1)
CORPORATE SOURCE: (1) Dep. Biol., Indiana Univ.-Purdue Univ. at Indianapolis, Indianapolis, IN 46202 USA
SOURCE: FEBS Letters, (1996) Vol. 392, No. 2, pp. 161-165.
ISSN: 0014-5793.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Regulation of sterol biosynthesis in the terminal portion of the pathway represents an efficient mechanism by which the cell can control the production of sterol without disturbing the production of other essential mevalonate pathway products. We demonstrate that mutations affecting early and late steps in sterol homeostasis modulate the expression of the ERG3 gene: a late step in sterol biosynthesis in yeast. Expression of ERG3 is increased in response to a mutation in the major ***isoform*** of ***HMG*** ***CoA*** reductase which catalyzes the rate-limiting step of sterol biosynthesis. Likewise, mutations in non-auxotrophic ergosterol biosynthetic genes downstream of squalene production (erg2, erg3, erg4, erg5, and erg6) result in an up-regulation of ERG3 expression. Deletion analysis of the ERG3 promoter identified two upstream activation sequences: UAS1, which when deleted reduces ERG3 gene expression 3-4-fold

but maintains sterol regulation and UAS2, which when deleted further reduces ERG3 expression and abolishes sterol regulation. The recent isolation of two yeast genes responsible for the esterification of intracellular sterol (ARE1 and ARE2) has enabled us to directly analyze the relationship between sterol esterification and de novo biosynthesis. Our results demonstrate that the absence of sterol esterification leads to a decrease in total intracellular sterol and ERG3 is a target of this negative regulation.

L15 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
ACCESSION NUMBER: 1995:179049 BIOSIS
DOCUMENT NUMBER: PREV199598193349
TITLE: ***HMG*** - ***CoA*** reductase and terpenoid phytoalexins: Molecular specialization within a complex pathway.
AUTHOR(S): Weissenborn, Deborah L. (1); Denbow, Cynthia J.; Laine, Marko; Lang, Saara S.; Yang, Zhenbiao; Yu, Xueshu; Cramer, Carole L. (1)
CORPORATE SOURCE: (1) Dep. Plant Pathol. Physiol. Weed Sci., Va. Polytech. Inst. State Univ., Blacksburg, VA 24061-0330 USA
SOURCE: Physiologia Plantarum, (1995) Vol. 93, No. 2, pp. 393-400. ISSN: 0031-9317.
DOCUMENT TYPE: General Review
LANGUAGE: English

AB Terpenoid phytoalexins and other defense compounds play an important role in disease resistance in a variety of ***plant*** families but have been most widely studied in solanaceous species. The rate-limiting step in terpenoid phytoalexin production is mediated by 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGR), which catalyzes mevalonic acid synthesis. HMGRs are involved in the biosynthesis of a broad array of terpenoid compounds, and distinct ***isoforms*** of HMGR may be critical in directing the flux of pathway intermediates into specific end products. ***Plant*** HMGRs are encoded by a small gene family, and genomic or cDNA sequences encoding HMGR have been isolated from several ***plant*** species. In ***tomato*** , four genes encode HMGR; these genes are differentially activated during development and stress responses. One gene, hmg2, is activated in response to wounding and a variety of pathogenic agents suggesting a role in sesquiterpene phytoalexin biosynthesis. In contrast, expression patterns of ***tomato*** hmg1 suggest a role in sterol biosynthesis and cell growth. Other ***plant*** species show an analogous separation of specific HMGR ***isoforms*** involved in growth and/or housekeeping function and inducible ***isoforms*** associated with biosynthesis of phytoalexins or other specialized "natural products." We are applying a variety of cell and molecular techniques to address whether subcellular localization and/or differential expression of these ***isoforms*** are key factors in determining end product accumulation during development and defense.

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